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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/276,868	03/26/1999	MICHAEL SIMONS	BIS-043	2716

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EXAMINER
KAM, CHIH MIN

ART UNIT	PAPER NUMBER
1653	18

DATE MAILED: 04/08/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/276,868	SIMONS ET AL.	
	Examiner	Art Unit	
	Chih-Min Kam	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the c rrespondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 January 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) *1-10* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Status of the Claims

1. Claims 1-15 are pending.

Applicants' amendment filed on July 23, 2001 (Paper No. 14) is acknowledged and applicant's response has been fully considered. Claims 1, 2, 6 and 11-15 have been amended. However, claims 1-10 are withdrawn from consideration due to restriction requirement (see section below) and claims 11-15 are under examination.

Election/Restrictions

2. Applicant's election with traverse of Group V, claims 11-15 in Paper No. 17 is acknowledged. Applicants urge that because all the claims have received two actions on the merit, it is now untimely, procedurally inappropriate, and blatantly unfair to impose a restriction requirement. The Examiner notes these arguments are presented throughout pages 2-9 of applicants' response. However, restriction can be imposed at any time during prosecution at the Examiner's discretion. As noted in the restriction requirement mailed October 9, 2001, there are at least five inventions, and applicants have not demonstrated that the inventions are not patentably distinct and there is no search burden to include additional groups. Restriction is proper when two or more claimed inventions are either independent **or** distinct. See MPEP 803. Furthermore, coexamination of each of the additional groups would have required a search of additional art areas. For example, including Group I, it would require additional searches for method of stimulating angiogenesis. Therefore, coexamination of each of these inventions would require a serious additional burden of search. It is the Examiner's opinion the prosecution will be advanced by examining a single invention at a time. Upon the allowance of

the product claims, the restriction requirement as to the inventions of process-making or process-using shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable product claim(s) will be entitled to examination in the instant application (see *In re Ochiai*, 71 F.3rd 1565, 37 USPQ2d 1127 (Fed. Cir. 1995)).

The requirement is still deemed proper and is therefore made FINAL.

Rejection Withdrawn

Claim Rejections – 35 USC § 112

3. The previous rejection of claims 11 and 15 under 35 USC § 112, first and second paragraphs regarding the term "functional" or "substantially" for lack description or introducing new matter, is withdrawn in view of applicants' amendment to the claims and applicants' response at pages 18-24 (Paper No. 14).

Claim Rejections - 35 USC § 102(a)/103(a)

4. The previous rejection of claims 11 and 15 under 35 U.S.C.102(a)/103(a) as being unpatentable by Blecha *et al.* (U.S.Patent 5,830,993), is withdrawn in view of applicants' amendment to the claims and applicants' response at pages 26-39 in Paper No. 14.

Informalities

5. The previous objection to the disclosure regarding providing "SEQ ID NO:" to the sequences in the specification, is withdrawn in view of applicants' amendment to the specification and applicants' response at page 8 (Paper No. 14). However, applicants insert "[SEQ ID NO:1]" at page 7, line 24 after "Fig. 10 presents Table 4", which is confusing as to whether "SEQ ID NO:1" is deleted or not because bracketing is commonly used to indicate a

deletion (see item no. 7). Appropriate correction is required. Use of "(SEQ ID NO:1)" is suggested. Please also make corrections at pages 23 and 25.

6. Please resubmit Fig. 9, which is missing in the application. Fig. 10 is objected to because "[SEQ ID NO:1]" has been used as a sequence identifier, which is confusing as to whether "SEQ ID NO:1" is deleted or not. Appropriate correction is required.

Claim Objections

7. Claim 11 is objected to because of the use the term "each member of said PR-39 derived oligopeptide family less than 26 amino acid residues in length;....". It appears "being:" between "family" and "less than" is missing.

8. Claims 12, 13 and 14 are objected to because of the use of "[SEQ ID NO:3]", "[SEQ ID NO:4]" or "[SEQ ID NO:5]". Bracketing or underlining are commonly used to indicate amendments or changes in the claims as provided in 37 CFR 1.121(a)(2)(ii) and are normally not intended to be printed in the published patent. In claims 12, 13 and 14, applicant has used "[SEQ ID NO:3]", "[SEQ ID NO:4]" or "[SEQ ID NO:5]" in such a manner that appears that the instant brackets would indicate deleted material and is thus, confusing as to whether "[SEQ ID NO:3]", "[SEQ ID NO:4]" or "[SEQ ID NO:5]" is included in the claim or not. The applicant can only amend by cancellation and presentation of a new claim. See also changes to 37 CFR 1.121 in Amendment rules package (Final Rule published on 8 Sep. 2000 (65 Fed. Reg. 54603), see also O. G. of 19 Sep. 2000 (1238 Off. Gaz. Pat. Office 77)).

Claim Rejections-Obviousness Type Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed.

Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

9. Claims 11-15 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 11-14 of copending Application No. 09/426,011. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 11-15 in the instant application disclose a family of PR-39 oligopeptides which are less than 26 or 20 amino acid residues, have Arg-Arg-Arg at N-terminus, are partially homologous to the native PR-39 peptide, can interact with $\alpha 7$ subunits of proteasomes, and can alter the proteolytic degradation activity of the proteasomes. This is obvious in view of claims 11-14 in the application (09/426,011) which discloses a family of PR-39 oligopeptides which are less than 26 amino acid residues, have Arg-Arg-Arg at N-terminus, are devoid of Pro-Pro-X-X-Pro-Pro-X-X-Pro and Pro-Pro-X-X-X-Pro-Pro-X-X-Pro where X is any amino acid, can interact in-situ with proteasomes in the cell, and can alter the proteolytic degradation of at least one identifiable peptide mediated by the interacting proteasomes. Since both sets of claims are directed to a family of PR-39 oligopeptides which are less than 26 amino acid residues and have Arg-Arg-Arg at N-terminus. Thus, claims 11-15 in present application and claims 11-14 in the application of 09/426,011 are obvious variations of a family of PR-39 oligopeptides which are less than 26 amino acid residues, have Arg-Arg-Arg at

N-terminus, can interact with α7 subunits of proteasomes, and can alter the proteolytic degradation activity of the proteasomes.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 11-15 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 11-15 are directed to a family of PR-39 oligopeptides which are less than 26 or 20 amino acid residues, have Arg-Arg-Arg at N-terminus, are partially homologous to the amino acid sequence of the native PR-39 peptide, can alter the proteolytic degradation activity of the proteasomes in-situ, can interact with in-situ α7 subunits of proteasomes, and can alter the proteolytic degradation activity of the proteasomes where the degradation activity of the proteasomes against one identifiable peptide (e.g., HIF-1α) is markedly inhibited while the degradation activity of proteasomes against other peptides remains unaltered. The specification, however, only discloses the full-length amino acid sequence of PR-39 have the properties of altering the proteolytic degradation activity of the proteasomes in-situ and interacting with α7

subunits of proteasomes (Examples 1-5), and PR11 (SEQ ID NO:4) is effective in stimulating angiogenesis in vivo (Example 7). There is no disclosure of any particular structure to function/activity relationship in the members of PR-39 derived oligopeptide family which are defined as all the previously unknown shorter-length homologs and analogs of native PR-39 such as PR-15, PR-11 and PR-8 (page 25; page 26, lines 2-4). Without guidance for structure to function/activity, one skilled in the art would not know which portions of the PR-39 are essential for function/activity to produce a functional polypeptide. The lack of a structure to function/activity relationship and the lack of representative species for the previously unknown shorter-length homologs as encompassed by the claims, applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise terms that a skilled artisan would not recognize applicants were in possession of the claimed invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 11-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 11-15 are indefinite because of the use of the terms "PR-39 derived oligopeptides", "at least one identifiable peptide", "at least partially homologous with ...PR-39 peptide", "markedly altering", "to interact in-situ with at least the α7 subunit of such proteasomes", "markedly inhibited" and "other individual peptides". The terms cited above render the claim indefinite, it is unclear how different the PR-39 oligopeptides are when

compared to the parent compound PR-39 as to "derived oligopeptides", how many identifiable peptides are intended and what the identifiable peptides are as to "at least one identifiable peptide", how much sequence homology the PR-39 oligopeptide has as compared to the native PR-39 and which part of the native PR-39 peptide the homology is referred to, to what extent the PR-39 peptide would alter the proteolytic degradation activity of proteasome as to "markedly altering", what other subunits of proteasomes would be interacted with PR-39 oligopeptide besides α7 subunit as to "at least the α7 subunit of such proteasomes", to what extent the proteolytic degradation activity of proteasome would be inhibited as to "markedly inhibited", and what sequences "other individual peptides" have. It is also unclear what "PR-39" stands for, a full spelled out word should be indicated in the first occurrence. Claims 12-14 are included in this rejection for being dependent on a rejected claim and not correcting the deficiency of the claim from which they depend.

Conclusion

12. No claims are allowed.

Art of Record

The following two references appear to be the closest art to the claimed invention. Bleccha *et al.* (U. S. Patent 5,830,993) teach antimicrobial peptide, PR-39 and its truncated peptides with N-terminal sequence (PR-26, PR-19 and PR-14), where PR-39 and PR-26 have antimicrobial activity, while the shorter peptide PR-14 does not have the antibacterial activity. However, the reference does not indicate the truncated peptides such as PR-19 and PR-14 can interact with α7 subunits of proteasomes and alter the proteolytic degradation activity of the proteasomes. Gallo *et al.* (U. S. Patent 5,654,273) teach PR-39 and its biological derivatives

have syndecan-inducing activity in mesenchymal cells and are useful in the modulation of wound healing and other disorders such as angiogenesis. However, the reference does not teach the PR-39 oligopeptides can interact with α7 subunits of proteasomes and alter the proteolytic degradation activity of the proteasomes.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (703) 308-9437. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (703) 308-2923. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-0294 for regular communications and (703) 308-4227 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Chih-Min Kam, Ph. D. CMK
Patent Examiner

KAREN COCHRANE CARLSON, PH.D
PRIMARY EXAMINER

March 31, 2002